

Hydroperoxides as Regulators of Calcium Release from Mitochondria

by

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During our studies on the mechanism of hydroperoxide-induced release of calcium from rat liver mitochondria we observed a hydrolysis of intramitochondrial pyridine nucleotides at the β -N-glycosidic bond between nicotinamide and ADP-ribose in intact mitochondria. The hydrolysis of NAD^+ is accompanied by a covalent modification of one protein at the inner side of the inner mitochondrial membrane by a ADP-ribose. Pyridine nucleotide hydrolysis, protein modification, and release of calcium from rat liver mitochondria are inhibited by ATP. Based on these findings we put forward the hypothesis that the covalent modification might be part of a mechanism controlling calcium release induced by hydroperoxides.

Autooxidation of linoleic acid induced

by xanthine oxidase

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The inclusion of polyunsaturated fatty acid hydroperoxides in linoleate micelles enhances the rate initiation of linoleate autooxidation induced by superoxide (HO_2^\cdot or $\text{O}_2^{\cdot-}$). This process is not iron dependent and singlet oxygen does not play a significant role. Iron chelates markedly enhance the rate of initiation, but this reaction probably proceeds by a different mechanism. We have examined the effects of various chelating agents on the reaction to better define the nature of the reaction we are studying. In addition, we have examined the effect of hydroperoxide structure on reactivity with superoxide.